

**Modulators of Receptors for Parathyroid Hormone
and Parathyroid Hormone-Related Protein**

Abstract

5 The present invention concerns therapeutic agents that modulate
the activity of PTH and PTHrP. In accordance with the present invention,
modulators of PTH and PTHrP comprise:

 (a) a PTH/PTHrP modulating domain; and
 (b) a vehicle, such as a polymer (e.g., PEG or dextran) or an Fc
10 domain, which is preferred;

 wherein the vehicle is covalently attached to the C-terminus of the
PTH/PTHrP modulating domain. The vehicle and the PTH/PTHrP
modulating domain may be linked through the N- or C-terminus of the
PTH/PTHrP modulating domain, as described further below. The
15 preferred vehicle is an Fc domain, and the preferred Fc domain is an IgG
Fc domain. Preferred PTH/PTHrP modulating domains comprise the PTH
and PTHrP-derived amino acid sequences described hereinafter. Other
PTH/PTHrP modulating domains can be generated by phage display,
RNA-peptide screening and the other techniques mentioned herein. Such
20 peptides typically will be modulators of both PTH activity and PTHrP
activity, although such techniques can be used to generate peptide
sequences that serve as selective modulators (e.g., agonists of PTH activity
but not PTHrP activity).